



TITLE:

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CITATION:

YAMAMOTO, Masanori ...[et al]. Comparison of enoxacin and norfloxacin in patients with cystitis. 泌尿器科紀要 1987, 33(12): 2141-2144

ISSUE DATE:

1987-12

URL:

<http://hdl.handle.net/2433/119370>

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COMPARISON OF ENOXACIN AND NORFLOXACIN IN PATIENTS WITH CYSTITIS

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The urinary antibacterial drugs enoxacin and norfloxacin were compared for efficacy and side effects in the treatment of lower urinary tract infections. Thirty-five patients received enoxacin and 25 received norfloxacin for one week. The antibacterial spectrum of enoxacin was noted to be better than that of norfloxacin, but both drugs performed well in clearing the infections caused by susceptible organisms. The incidence of side effects was higher with norfloxacin than with enoxacin.

Key words: Cystitis, Enoxacin, Norfloxacin

INTRODUCTION

For an antimicrobial agent to be useful in the treatment of urinary tract infections, in addition to being relatively nontoxic and well tolerated, it should achieve high urinary concentrations of biologically active drug¹⁾, concentrations which are many times higher than the minimal inhibitory concentrations (MIC) of the infecting organism.

One of the newer oral preparations which appears to meet these therapeutic requirements is the synthetic antibacterial drug enoxacin. Enoxacin is similar to norfloxacin with activity against most common organisms associated with urinary tract infections^{2~3)}. Its antimicrobial activity is similar to that of norfloxacin, but it has been more effective than norfloxacin against *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Serratia marcescens* and *Pseudomonas aeruginosa* in infected mouse⁴⁾. Enoxacin is cleared from the body predominantly by renal excretion, and to a smaller extent by metabolism⁵⁾. The urinary concentration of enoxacin exceeds that achieved by an equivalent dose of norfloxacin^{5~6)}. We have used enoxacin in patients with cystitis, comparing its safety

and effectiveness with that of norfloxacin.

MATERIALS AND METHODS

The study group consisted of 60 patients, 51 women and 9 men, between 18 and 75 years old. Five patients (4 on enoxacin, 1 on norfloxacin) were found to have asymptomatic bacteriuria and the other 55 were diagnosed as having cystitis, either initial or recurrent, uncomplicated, or complicated if the integrity of the urinary tract was impaired. Pregnant patients were excluded as were those who had received successful antibacterial therapy before administration of the study drug.

On admission, all patients gave a complete history and received a thorough physical examination. Urine was obtained for culture, organism identification, colony count, and antimicrobial susceptibility, and blood was obtained for routine hematologic and biochemical screening. Treatment was then started with either 600 mg enoxacin, or 600 mg norfloxacin, the drugs being assigned by a predetermined random code and administered three times daily for one week. Further urine cultures were obtained 3 to 5 days after starting treatment and 7 to 9 days after

treatment ended. Any adverse reactions noticed by the patients were recorded, and standard laboratory tests of hematologic, renal and hepatic functions were repeated at the end of therapy. *In vitro* susceptibility of the infecting organism to the study drugs was determined by the disk method.

RESULTS

Table 1 shows the infecting organism for each patient. As would be expected, *Escherichia coli* was identified most frequently (54.3%). Clinical evaluation was made according to the Criteria for Clinical Efficacy of Antimicrobial Agents on Urinary Tract Infection (2nd Edition).

Table 1. Isolated organisms in each drug group (over 10^5 colony-forming units/ml.).

Pathogen	No.	Pathogen Eliminated No.	%
ENOXACIN			
<i>E. coli</i>	19	18	94.7
<i>K. pneumoniae</i>	8	7	87.5
<i>Enterobacter</i>	4	3	75
<i>S. aureus</i>	1	1	100
<i>S. epidermidis</i>	1	1	100
<i>P. aeruginosa</i>	1	0	0
<i>S. marcescens</i>	1	0	0
TOTALS	35	30	
NORFLOXACIN			
<i>E. coli</i>	15	14	93.3
<i>P. mirabilis</i>	3	2	66.7
<i>P. vulgaris</i>	2	2	100
<i>S. faecalis</i>	1	1	100
<i>Morganella</i>	1	1	100
<i>Enterococcus</i>	1	1	100
<i>K. pneumoniae</i>	1	0	0
<i>P. aeruginosa</i>	1	0	0
TOTALS	25	21	

Enoxacin-treated group consisted of 26 cases of acute simple cystitis and 9 cases of chronic complicated cystitis. In the case of acute simple cystitis, pyuria was cleared in 24 cases (92.3%) and bacteriuria was completely eliminated in 25 cases (96.1%). Overall clinical efficacy was 97.2%. In the case of chronic complicated cystitis, pyuria was cleared in 2 cases (22.2%) and decreased in 6 cases (67%); bacteriuria was completely eliminated in 5 cases (55.6%) and overall clinical efficacy was 77.8%. In one instance, the initial pathogen was not eliminated despite

a satisfactory symptomatic response, and this was a 58-year-old man with initial, complicated cystitis caused by *P. aeruginosa*, who had been treated for 16 days. The norfloxacin-treated group consisted of 20 cases of acute simple cystitis and 5 cases of chronic complicated cystitis. Of the patients with acute simple cystitis, pyuria was cleared in 18 cases (90%) and bacteriuria was completely eliminated in 19 cases (95%). The overall clinical efficacy was 96.8%. Of the patients with chronic complicated cystitis, pyuria was cleared in 1 case (20%) and decreased in 1 case (20%); bacteriuria was completely eliminated in 2 cases (40%) and overall clinical efficacy was 60%. One patient had a recurrence of symptoms although the pathogen was eliminated, and one became reinfected with a different pathogen.

All 60 patients were evaluated for the occurrence of adverse drug reactions. In the enoxacin-treated group, 3 female patients (8.57%) had adverse reactions, but these side effects were reversible. One patient was found to have a slight elevation of alkaline phosphatase on occasion, but no symptomatic complaints. In the norfloxacin-treated group, there were 4 patients (female) with adverse reactions (16%). None of these symptoms were so severe as to necessitate discontinuation of therapy and vanished after cessation of treatment of norfloxacin. One patient was found to have a slight elevation of serum GOT level on occasion, but this was transient and the patient was asymptomatic.

Table 2. Adverse reactions in each drug treatment group.

Side effects	No. of Cases
ENOXACIN	
Nausea	1
Vomiting	1
Elevation of alkaline phosphatase	1
NORFLOXACIN	
Nausea	1
Headache	1
Sleepiness	1
Elevation of serum GOT	1

matic. Table 2 shows the adverse reactions that were noticed.

DISCUSSION

It is apparent from the present results that both enoxacin and norfloxacin are effective antibacterial agents for the treatment of simple or complicated cystitis. The incidence of side effects was higher with norfloxacin than with enoxacin.

Enoxacin is a newly developed synthetic antimicrobial agent that is a pyridone-carboxylic acid derivative. This drug as well as norfloxacin has broad and potent antibacterial activities against gram-positive and gram-negative bacteria, and shows excellent oral effects in various experimental infections (systemic, pulmonary, dermal and urinary tract infections) in mice⁴⁾. Enoxacin is similar to norfloxacin in *in vitro* antibacterial properties but superior to norfloxacin in *in vivo* antibacterial activities⁴⁾. The wider antibacterial spectrum of enoxacin will make it a valuable drug for the treatment of infections due to *E. coli* or *Proteus* organisms. *E. coli* now ranks as the first most prevalent pathogen isolated from nosocomial urinary tract infections in our hospital. Until now we have had a choice only between pipemidic acid or a broad-spectrum antibiotic for treatment of this type of infection. As a result of the widespread, and sometimes long-term use of pipemidic acid, resistant strains of *E. coli*, as well as of *Proteus*, *Klebsiella* and *Enterobacter* are now beginning to emerge, so that the arrival of this new drug is particularly opportune.

Although for the purpose of this study, both drugs were given on the same three-times-daily basis, enoxacin has a further advantage in being equally effective on a twice-a-day basis⁷⁻⁹⁾, which will improve patient compliance with the prescription regimen. Enoxacin's effectiveness and lack

of unpleasant side effects should make it a drug of first choice in the treatment of lower urinary tract infections.

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(Accepted for publication July 2, 1987)

和文抄録

膀胱炎患者に対する **Enoxacin** と **Norfloxacin** の効果に関する比較検討

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橋 本 純 一・三 宅 弘 治

尿路抗菌剤であるエノキサシンとノルフロキサシンの下部尿路感染症に対する臨床効果と副作用に関する比較検討を行なった。35人の患者にはエノキサシンを、25人の患者にはノルフロキサシンをそれぞれ1週間投与した。エノキサシンの抗菌スペクトラムは、ノ

ルフロキサシンよりも優れていたが、両剤とも、感受性菌による感染症には良好な成績をおさめた。副作用の頻度は、ノルフロキサシンの方がエノキサシンよりも高かった。